REMARKS

By way of the present amendment, claims 16-21, 25-27, 30-41 and 45-50 are pending. Claims 21, 25, 26, 30, 36, and 39 have been amended without prejudice, and claims 45-50 have been added. Support for the new and amended claims can be found throughout the specification and in the claims as originally filed, for example, on page 15, lines 11-22; and page 22, lines 7-9. No new matter enters by way of these amendments.

I. Rejections under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 21, 25-27 and 30-41 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention at the time the application was filed. Office Action at page 2. More particularly, the Examiner alleges that "[t]here is no correlation between the structure of HES 1 from yeast and any discrete function that is required for adequate written description of a genus." *Id.* Applicants respectfully disagree.

At the outset, such a rejection is <u>not</u> applicable to claims 25-27 and 36-37 which are directed to a plant or a method of making a plant with a particular nucleic acid sequence as none of these claims recite "HES 1". As such, the Examiner's concern regarding adequate written description of a genus is inapplicable to such claims.

Moreover, Applicants have described the claims that recite HES 1. A genus of nucleic acids may be described by a structural feature that distinguishes members of the claimed genus from non-members of the claimed genus. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Applicants have satisfied this test for written description. Applicants have provided a structural feature, the nucleotide sequence of SEQ ID NO: 4 as well as the corresponding amino acid sequence, SEQ ID NO: 33. These features provide a basis for each and every nucleic acid molecule in the claimed genus. Furthermore, it distinguishes

the members of the claimed genus from non-members. In contrast to the mere name "cDNA" as provided in *Eli Lilly*, Applicants have provided detailed chemical structures.[1]

The Examiner also suggests that there are no relevant identifying features because the yeast HES 1 protein and the maize HES 1 protein are asserted to not have the same number of amino acids and to have gaps in the sequence comparison. Applicants disagree with the Examiner's conclusion. A BLAST algorithm using SEQ ID NO: 33 provides a list of several other members of the oxysterol binding protein family. Clearly, SEQ ID NO: 33 has at least one relevant structural feature, its sequence, that links these respective nucleic acid sequences. Moreover, the specification describes the identification of these sequences using a nucleic acid sequence encoding HES 1 from yeast. *See, e.g.,* Specification at page 61, line 22 through page 62, line 5.

Based on Applicants' disclosure, one of ordinary skill in the art would recognize that Applicants were in possession of the claimed invention at the time of filing. Therefore, Applicants respectfully request reconsideration and withdrawal of the written description rejection of claims 21, 25-27 and 30-41 under 35 U.S.C. §112, first paragraph.

II. Rejections under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 16-21, 25-27 and 30-41 stand rejected under 35 USC § 112, first paragraph, as allegedly containing "subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Office Action at page 3. In particular, the Office Action asserts that "Applicant's disclosure provides no working examples of a plant HES 1 protein or what phenotype one of skill in the art

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[1] In a recent decision, the Federal Circuit considered the written description requirement for biochemical processes, including gene modification and protein expression, and held that generic inventions may be adequately supported even without a DNA sequence of the claimed subject matter. *See Capon, et al. v. Eshhar, et al.*, Appeal Nos. 03-1480, -1481, Slip op. page 15 (Fed. Cir. August 12, 2005). *See also, In re Wallach*, 378 F.3d 1330, 1333-34 (Fed. Cir. 2004) (an amino acid sequence supports the entire genus of DNA sequences that encode the amino acid sequence).

could expect to produce when transforming a plant with any one of the claimed sequences." *Id.* Applicants respectfully disagree.

At the outset, such a rejection is not applicable to claims 16 and 17 which recite a substantially purified nucleic acid molecule that encodes a particular amino acid sequence. Neither of these claims recite "HES 1" and as such, the Examiner's concern that "computer analysis of nucleic acid sequences is unpredictable" is inapplicable to these claims. For similar reasons, the Examiner's rejection of claims 18-20, 25-27 and 36-38 is inapplicable and should be withdrawn.

Moreover, claims reciting HES 1 are enabled.[2] For example, the specification teaches plant nucleic acid sequences encoding HES 1 (including SEQ ID NO: 4) as well as the encoded amino acid sequences (including SEQ ID NO: 33). *See, e.g.*, specification at page 12 line 10 through page 18, line 27; page 18, line 29 through page 21, line 2; and in the Sequence Listing. In addition, claims reciting HES 1 recite that the nucleic acid sequence of a HES 1 protein has between 100% and 95% sequence identity with a nucleic acid sequence of SEQ ID NO: 4 or a complement thereof. Given the skill in the art and such a characterization of HES 1, claims reciting HES 1 are enabled.

The Examiner also argues that "the lack of guidance and working examples in the specification combined with the state of the art would require that one of skill in the art perform undue trial and error experimentation, transforming a multitude of plants with a multitude of non-exemplified nucleic acid sequence[s] to retrieve a non-specified phenotype." Office Action at page 4. Applicants disagree. In particular, the Examiner's concern that "Applicant's disclosure provides no working examples of a plant HES 1 protein or what phenotype one of skill in the art could expect to produce when transforming a plant with any one of the claimed sequences" is <u>not</u> a proper basis upon which claims 16-20, 25-26, 36-37, or 45-50 could be rejected.[3] *Id.* at 3.

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[2] Claims 21, 30-35, 39-41, and 49 recite a HES 1 protein.

[3] None of these claims recite a phenotype, and as such, the Examiner's rejection based on the phenotype being "non-specified" is inapplicable to these claims.

In particular, claims directed to a plant expressing a specific protein are enabled. In light of the specification, reducing the claimed invention to practice is routine in the art. For example, the specification teaches plant nucleic acid sequences encoding HES 1 (including SEQ ID NO: 4) as well as the encoded amino acid sequences (including SEQ ID NO: 33). *See, e.g.*, specification at page 12 line 10 through page 18, line 27; page 18, line 29 through page 21, line 2; and in the Sequence Listing. Moreover, the specification provides guidance for the preparation of constructs for use in plant transformation methods, as well as methods for the transformation of plants using the constructs. *See, e.g.*, Specification at page 21, line 3 through page 35, line 23. Furthermore, the specification provides methods for assaying gene function in yeast. *See, e.g.*, Example 1 at pages 60-61. In addition, techniques for transformation of a nucleic acid construct into a plant are well-known in the art. As such, claims 25-26, 36-37, and 50 are fully enabled.

The Examiner also suggests that HES 1 alone would not produce a detectable phenotype in a transformed plant. *Id.* at 4. At the outset, Applicants note that only claims 21, 27, 32, 38, and 41 are directed to a plant having increased phytosterol levels. With respect to these claims, nothing in Fang *et al.* suggests that the HES 1 proteins encoded by the nucleic acid sequences of the present invention could not be used to modulate phytosterol biosynthesis in a plant cell. As such, the Examiner's reliance on Fang *et al.* for this enablement rejection is misplaced. In fact, several studies have been reported since Applicant's filing date to support the role of HES 1 and its homologues in transport of lipids and regulation of sterol homeostasis.[4]

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[4] The Examiner's attention is further directed to Hynynen, *et al.*, *Biochem. J.* (2005) 390:273-283; Im *et al.*, *Nature* (2005) 437:154-158; and Levine, (2005) 19:722-723. *See* references attached to Form PTO-1449 submitted herewith. For example, Im *et al.*, states that OSBP-related proteins (the ORPs) are essential for life in eukaryotes. Im *et al.*, at page 154 column 1, first paragraph after abstract. Further, Levine refers to large families of ORPs in humans, yeast, or plants (six genes in *Arabidopsis thaliana*). *See* Levine at page 722 (Figure 1). Such disclosures, and there are numerous in the published art, support Applicants claims such that the asserted gaps in sequence alignment alleged by the Examiner are inconsequential.

Accordingly, for at least these reasons, the enablement rejection under 35 USC § 112, first paragraph, is traversed, and reconsideration and withdrawal of this rejection is respectfully requested.

IV. Rejections for Double Patenting

Claims 16, 17, and 25 stand provisionally rejected under 35 USC § 101, double patenting, as allegedly containing the same invention as that of Claims 28-29 and 39, respectively, of copending Application No. 10/793,639. Office Action at page 6. Claims 16-21, 25-26 and 28-29 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting, for allegedly containing the same invention as that of Claims 28-41 of copending Application No. 10/793,639.

Since the mailing of this Office Action, copending Application No. 10/793,639 has gone abandoned, and for at least these reasons, the double patenting rejections are now moot. As such, Applicants respectfully request withdrawal of this rejection.

Conclusion

In view of the foregoing remarks, Applicants respectfully submit that the present application is now in condition for allowance, and notice of such is respectfully requested. The Examiner is encouraged to contact the undersigned should any additional information be necessary for allowance.

Respectfully submitted,

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